Phlegmonous gastritis after endoscopic submucosal dissection for early gastric cancer

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Abstract: A 74-year-old man with diabetic nephropathy developed epigastric pain and high fever after endoscopic submucosal dissection (ESD) for early gastric cancer. Gastroscopy, endoscopic ultrasonography and computed tomography showed ulceration with a purulent lake, thickened entire gastric mucosal layers suggesting focal abscess formation, leading to the diagnosis of phlegmonous gastritis. He underwent total gastrectomy as an emergency. Histological findings of the resected specimen showed severe inflammatory cell infiltration and multiple focal abscess formation spreading to the entire gastric wall. In patients with poorer general conditions, phlegmonous gastritis should be considered as a serious complication after ESD, indicating a requirement of antibiotic prophylaxis.

Keywords: Phlegmonous gastritis, severe complication, early gastric cancer, endoscopic submucosal dissection

Introduction

Gastric cancer is one of the most prevalent malignancies in the world. Recent developments in endoscopic procedures can improve patient care in early gastric cancer [Ohkuwa *et al.* 2001; Yamamoto *et al.* 2001; Yamamoto *et al.* 2002; Miyamoto *et al.* 2002]. Endoscopic submucosal dissection (ESD) has been developed as one of the new therapeutic modalities for early gastric cancer and is considered to be a relatively safe method with low invasiveness [Miyamoto *et al.* 2002; Yamamoto *et al.* 2002]. Although bleeding and perforation are the most frequent complications associated with ESD, these can be adequately managed without surgical intervention in most cases and other serious complications are considered to be rare.

Phlegmonous gastritis is an uncommon, often fatal condition characterized by suppurative bacterial infection of the stomach [Kim *et al.* 2005]. It may arise from a local or a disseminated haematogenous infection and may involve either a portion of the stomach (localized type) or the entire stomach (diffuse type). Here we report a rare case with phlegmonous gastritis, developed

after ESD for early gastric cancer. The patient was treated initially with antibiotic therapy but required surgery on emergency. Phlegmonous gastritis should be recognized as a severe complication after ESD and in cases with immune compromised states we should take precautions against its development.

Case report

A 74-year-old man with diabetic nephropathy was introduced to our hospital to treat early gastric cancer. He had a depressed-type early gastric cancer in the antrum. Pathological diagnosis of the lesion was papillary adenocarcinoma (Figure 1a). The flexible spectral imaging colour enhancement (FICE) named by the Japanese Society of Spectral Imaging for endoscopy in June 2008 showed a clear demarcation line between the cancerous lesion and the surrounding area, (Figures 1b and 1c) [Osawa *et al.* 2008] and the endoscopic ultrasonography (EUS) showed a cancer lesion confined within the mucosal layer, fulfilling the extended criteria for ESD [Gotoda *et al.* 2006]. Therefore, the patient was scheduled to undergo ESD.

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Figure 1. Conventional endoscopic image (a) and FICE image (b) of the slightly depressed lesion in the antrum. FICE showed a clear demarcation line between the cancerous lesion and the surrounding area. A 40-fold magnified FICE image (c) showed an irregular microstructural pattern, suggestive of gastric cancer. The ulceration after ESD using sodium hyaluronate solution (d).

The patient had been having haemodialysis for 15 years because of diabetic nephropathy. He had a moderate anaemia with 9.7 g/dl of haemoglobin concentration, a lower level of platelet count and white blood cells, 111,000/ μ l and 3400/ μ l, respectively, but levels of coagulation factors were normal. Blood chemistry data on admission were normal except for renal functions. He had undergone ESD using sodium hyaluronate solution without any technical problems (Figure 1d). The size of the mucosa resected en bloc was 59 $\times$ 27 mm in diameter including 40 $\times$ 11 mm of cancer lesion. Five hours later, he complained of epigastric pain and on the next day he developed high fever of 39°C and vomited a small amount of blood. Endoscopic examination showed large coagulation and protruded vessels in the ulceration after ESD, which was treated with endoscopic coagulation therapy. He began to eat soft meals from two days after ESD, but the epigastric pain and signs of rebound tenderness continued. He had high fever of 39°C again

from the five days after ESD and higher levels of CRP (30 mg/ml). Computed tomography (CT) showed a thickened gastric wall along the antral area, suspicious of phlegmonous gastritis (Figure 2d). The endoscopic examination on the seven days after ESD showed oedematous mucosa and ulceration with a yellowish purulent lake. (Figure 2a and b). EUS showed a diffusely thickened gastric wall extending to the muscle layers, suspicious of abscess formation (Figure 2c).

Citrobacter freundii, *Enterobacter cloacae* and α -*Streptococcus* were cultured from his gastric secretion. The epigastric pain and high fever then transiently disappeared after antibiotic treatment with flomoxef (FMOX 0.5g/day), but relapsed 10 days later. CT showed a thickened gastric wall extending to subserosa with multiple low density areas suspicious of focal abscess formation and impending perforation (Figure 3c). The endoscopic examination revealed diffuse ulceration with a massive purulent lake, strongly

Figure 2. The ulceration on the seven days after ESD was enlarged and covered by yellowish purulent mucus (a). The gastric mucosa was diffusely oedematous and new ulceration was visualized in the middle body (b). EUS showed a thickened and irregular hyperechoic third layer corresponding to the submucosal layer on the greater curvature (c). Abdominal CT revealed a diffusely thickened gastric wall, suggesting phlegmonous gastritis (d).

Figure 3. Endoscopic examination showed the massive purulent lake in the stomach (a) and the diffuse ulceration extended to the proximal part of the stomach (b) on the 17 days after ESD. CT showed a thickened gastric wall with multiple low density areas suggestive of focal abscess formation approximating submucosa (c).

Figure 4. Postoperative histological views (hematoxylin and eosin) of the mucosa (a), submucosa and upper muscular layer (b), and serosa (c), showing acute suppurative gastritis with multifocal abscess formation and infiltration of inflammatory cells in all layers of the stomach.

indicating a high risk of perforation and sepsis in agreement with the CT findings (Figure 3a and b). Thus, he underwent total gastrectomy on emergency. Histological findings of the resected specimen were consistent with phlegmonous gastritis with severe inflammatory cell infiltration and multiple focal abscess formation in the entire gastric wall, but no perforation. (Figure 4a–c) He recovered uneventfully after gastrectomy.

Discussion

In this report, we present a case with phlegmonous gastritis as a rare and severe complication after ESD. This is the first report of phlegmonous gastritis after ESD for early gastric cancer. Phlegmonous gastritis, although a rare condition, is a submucosal bacterial infection with characteristic macroscopic and histological findings. Endoscopy, EUS and CT are useful in the diagnosis of phlegmonous gastritis [Danny *et al.* 2000; Sood *et al.* 2000; Iwakiri *et al.* 1999]. The most common pathogens responsible for phlegmonous gastritis are *Streptococcus spp*, *Staphylococcus spp*,

Escherichia coli, *Haemophilus influenza*, *Proteus*, and *Clostridia* [Miller AI *et al.* 1975; Schultz *et al.* 1996; Stephenson *et al.* 1970]. *Citrobacter freundii* isolated from gastric mucus in the present case has never been reported before. This bacterium is a member of the family *Enterobacteriaceae* and is often the cause of significant opportunistic infections. *C. freundii* has been associated with neonatal meningitis and brain abscess, [Joaquin *et al.* 1991] and could be responsible for phlegmonous gastritis in our case. The natural history of phlegmonous gastritis is that it deteriorates gradually leading to a life-threatening condition; the mortality rate of patients medically treated for the focal type is 17%, and for the diffuse type is 60% [Kim *et al.* 2005]. Therefore, the combination of early radical gastric resection and vigorous antibiotic therapy appears to be the treatment of choice in phlegmonous gastritis [Lee *et al.* 2005; Yokota *et al.* 2005]. Such a clinical course was consistent with our case.

In previous literature, the causative factors of phlegmonous gastritis have included predisposing

factors such as severe alcoholism, gastric haemorrhage, achlorhydria, and mucosal injury, acquired immune deficiency syndrome, and also after endoscopy [Hommel *et al.* 2007; Iwakiri *et al.* 1999; Kim *et al.* 2005; Lee *et al.* 2005]. Our patient had diabetic nephropathy and chronic severe atrophic gastritis that might induce lower gastric acid production. In patients with such underlying conditions, we must be more cautious of the risk of phlegmonous gastritis after ESD. However it is noteworthy that even without such apparent underlying conditions, phlegmonous gastritis develops after endoscopic procedures. Bron *et al.* reported on a patient who developed phlegmonous gastritis after endoscopic snare biopsy [Bron *et al.* 1977]. Another case of phlegmonous gastritis after endoscopic mucosal resection (EMR) of smaller size that required total gastrectomy has been reported [Lee *et al.* 2005]. Since post-ESD ulceration tends to be larger than post-EMR ulceration, the present case with diabetic nephropathy might be a high risk for phlegmonous gastritis. With the advent of the ESD technique, early gastric cancer with a diameter greater than 30 mm has been treated in Japan [Yamamoto *et al.* 2001]. In patients with poorer general conditions, administration of proper antibiotics should be considered to prevent phlegmonous gastritis after ESD.

Conflict of interest statement

None declared.

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